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March 17, 1999

Dockets Management Branch
HFA- 305
Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, Maryland 20852

Re: Docket No. 98N-0182 List of Bulk Drug Substances That May Be Used in Pharmacy Compounding

The American Academy of Dermatology (the Academy) strongly supports the proposed inclusion on the list of bulk drug substances that may be used in pharmacy compounding of cantharidin for topical use in the professional office setting. This substance has been used by dermatologists in the office setting for over 25 years and has been particularly efficacious in the treatment of molluscum contagiosum in young children. The Academy also supports the inclusion of ferric subsulfate and ferric sulfate hydrate for topical use only.

The Academy provides the following information in support of inclusion of the topical sensitizers dinitrochlorobenzene (DNCB), diphencyclopropenone (DCPC), and squaric acid dibutyl ester (SADBE) on the list of bulk drug substances that may be used in pharmacy compounding. Our comments will not address the criterion of the chemical characterization of these substances, as the proposed rule states that these three substances are well characterized chemically.

Since 1976 topical sensitizers have been used in the treatment of alopecia areata that is unresponsive to traditional treatment. There are varying theories on the mechanism of action, but none are based on strong scientific evidence. Patients are treated topically with these substances at a concentration to maintain a mild contact dermatitis. Consequently, dilution of the solution may be required dependent on patient response.

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The efficacy of these substances has been associated with several factors including type of alopecia and extent of hair loss, duration of disease, age at onset, and family history of alopecia areata. Relapse is not uncommon, and reports of long-term follow-up are few. Nevertheless, these substances can be effective for certain patients with disease that is recalcitrant to other forms of therapy.

The safety of these substances has been established through several studies, i.e., DNCB (*Weisburger, et al*), SADBE (*Feldman, et al*), and DPCP (*Wilkerson, et al,* and *Stute, et al).*

These substances are obviously not first line therapy for the treatment of alopecia. Their availability through listing on the bulk substances drug list will allow dermatologists the flexibility to continue to offer patients an alternative therapy that may be effective when no other treatment has helped.

Sincerely,

Lynn A. Drake, M.D.
President

References

Rokhsar CK, et al. Efficacy of topical sensitizers in the treatment of alopecia areata. J Am Acad Dermatol 1998;39:751-61.

Weisburger EK, et al. Testing of twenty-one environmental aromatic amines or derivatives for long-term toxicity or carcinogenicity. J Environ Pathol Toxicol 1978;2:325-56.

Feldman, et al. Absorption of some organic compounds through the skin in man. J Invest Dermatol 1970;54:399-404.

Wilkerson M, et al. Assessment of diphenylcyclopropenone for photochemically induced mutagenicity in the Ames assay. J Am Acad Dermatol 1987;17:606-11.

Stute J, et al. Diphenylcyclopropenone: a new strong contact sensitizer. Dermatol Beruf Umwelt 1981;29:12-4. (Author's translation)

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